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AN EPIDEMIC OF NOMA.

By HAROLD NEUHOFF, M.D.,

ADJUNCT SURGEON TO THE NEW YORK HEBREW INFANT ASYLUM.

THROUGH the kindness of Dr. Jonas E. Reinthaler and Dr. Charles A. Elsberg, respectively attending physician and surgeon to the New York Hebrew Infant Asylum, I had the opportunity of studying an epidemic of noma which occurred in that institution in the spring of 1909. The asylum is a substantial, well-preserved edifice. It was originally a private dwelling, and was later enlarged by the addition of wings. The institution accommodates about 150 children. During the epidemic there were 140 children in the asylum of varying ages, up to six years.

Three cases of noma occurred in the asylum during fourteen years, one in November, 1902, one in February, 1907, and one in February, 1908. All three patients died; in two the treatment was conservative; in the third and last a wide excision was performed by Dr. Elsberg. In the three cases the disease developed in the course of epidemics of measles complicated by ulcerative stomatitis. It is of interest that the three cases, though widely separated in time, occurred in the same ward—a sunny, well-ventilated room.

The epidemic of noma of 1909 complicated an epidemic of measles, which spread in the institution despite careful isolation of all the exposed children. The epidemic of measles was a severe one and complications were frequent. There were 81 cases—of which 13 developed diphtheria, and 24 pneumonia—with a mortality (exclusive of noma) of 4 per cent. Although special attention was paid to the mouths, ulcerative stomatitis occurred in fully 25 per cent. of the children, and it was among these children that most of the cases of noma developed. There were 8 cases of true noma and 3 doubtful ones, to which reference will later be made.

One of the most striking facts about noma is that it has formerly broken out, almost invariably, in overcrowded and ill-regulated hospitals. For example, Saviard and Poupart¹ recorded epidemics of noma in the old Hôtel Dieu in Paris under such circumstances; in the new institution the disease did not develop. There are many similar reports in the literature of the disease. On the other hand,

¹ Trans. Med. Chir. Soc., Edinburgh, 1802-9, xii, 251.

in recent years epidemics have broken out in excellent institutions, as in that reported by Blumer and McParlane² and in that of Crandon, Place, and Brown.³

The association of noma with the infectious diseases—especially measles and pertussis—is well known. The pronounced tendency for noma to appear in the spring and fall may depend upon the greater frequency of the infectious diseases in those seasons. There is no conclusive proof that the disease is contagious. Mayr⁴ believes in its contagiousness; Holt⁵ is of the same opinion, as he has seen 5 cases of noma, after whooping cough, develop in the same ward. Of the cases in our epidemic, 2 developed in one ward, 3 appeared in another, and 5 (including the three not proved) developed in a third ward, which was reserved, as far as possible, for all of the cases of stomatitis. A single case developed in the isolation house to which the child, suffering from diphtheria, had been transferred. Two of the wards were on the same floor, the third was on another. Each ward was carefully isolated, had its special nurses, separate food, dishes, etc. The children who developed noma were transferred to the isolation house as soon as the disease appeared. It is often impossible to say when noma is developing, and undoubtedly many children were exposed to the disease when they were presumably in a receptive condition—suffering from measles and ulcerative stomatitis. With these conditions, favorable for the spread of a contagious disease, only a few of the little patients were attacked by noma, and no connection could be demonstrated between the isolated cases.⁶

Noma may appear at any age and among all cases of patients. The large majority of the cases have occurred among poorly nourished children⁷ during the first and second dentition, and many apparently developed from ulcers around the teeth. Rilliet and Barthez,⁸ in their classic description of the disease, describe noma in infants at the breast. Inasmuch as noma so often follows ulcerative stomatitis, many writers (Richhorst,⁹ Henoch,¹⁰ Guizetti,¹¹ Seiffert,¹² etc.) consider noma an advanced stage of stomatitis. They point out that at first it is a purely local disease, that the same organisms

² AMER. JOUR. MED. SCI., 1901, cxxii.

³ Boston Med. and Surg. Jour., April 15, 1909.

⁴ Zeitschr. der Knis.-Kön. Gesellsch. der Aerzte zu Wien, 1852.

⁵ Diseases of Infancy and Childhood, 1905, pp. 200, 692.

⁶ Schmorl (Zeitschr. f. Tiermed., 1891, p. 375) described an epidemic, among rabbits, of gangrene beginning in the mouth, which was very similar to noma. He showed that it was contagious.

⁷ Some of these cases in the literature described as noma in adults correspond very closely to cases of leukæmia with terminal gangrenous ulceration in the mouth. Blood examinations were not recorded.

⁸ Traité des Malad. des Enfants, 1852, p. 62.

⁹ Specielle Patholog. und. Therap.

¹⁰ Trans. Chicago Path. Soc., 1896, i, 252. †

¹¹ Il Policlinico, 1899.

¹² Münch. med. Woch., 1901.

are found in the smears taken from the ulcers of both diseases, and that the transition from the one condition to the other has been observed. It will be shown below that a definite bacteriological picture is found in noma and not in ulcerative stomatitis.

There are usually no constitutional symptoms until the gangrene has begun to spread. The child is usually quiet and languid, but may be very restless and irritable. Often it is profoundly prostrated, but may feel well enough to sit up in bed and play, although the gangrene is spreading over its face. Marked pallor is an early symptom. The pulse soon becomes rapid and small; there is slight or no fever, and generally no pain. Thirst is marked, although the tongue is moist. Diarrhœa is often a serious symptom, but, according to some observers, occurs only when gangrenous material is swallowed.¹³ Bronchopneumonia is the most frequent and fatal complication. It is of the aspiration type, and not uncommonly leads to abscess or gangrene of the lung.

Of the physical signs, the ulcer is usually the first lesion observed (Bohn,¹⁴ Eichhorst, Osler,¹⁵ etc.). Billroth, however, describes a nodule in the cheek as the starting point, and Fagge¹⁶ believes the disease begins immediately under the mucous membrane. The necrotic ulcer becomes gangrenous, the adjoining portion of the cheek becomes intensely infiltrated, and the gangrene extends to it and often to the adjacent maxilla. The peculiarly penetrating foul odor from the mouth is at the beginning faint, yet it may be the first sign to call attention to the disease. As the overlying skin becomes involved, it assumes a violaceous hue, later turns black and is covered with vesicles; finally the gangrenous ulcer breaks through. Tourdes¹⁷ describes three stages of the disease: (1) Ulceration of the mucous membrane, œdema of the face, infiltration of the cheek, lasting two or three days; (2) gangrene, lasting five to twelve days; and (3) the period of general infection. Rarely the disease runs a subacute course over several months. Finally, Gierke noted that noma may recur.¹⁸

In a large number of cases collected from the literature the mortality ranged from 70 to 100 per cent.

Many different kinds of treatment have been recommended.

¹³ Several autopsies have shown a gangrenous condition of the gastro-intestinal tract. In 8 cases of noma of the genitalia and of the external ear observed by Gierke (Jahrb. f. Kinderheilk., 1898, p. 65) diarrhœa was present in only one case, and then it was of short duration.

¹⁴ Gerhard's Handb. der Kinderk., iv.

¹⁵ Practice of Medicine, 1905.

¹⁶ Amer. System of Diseases of Children.

¹⁷ Thèse de Strassbourg, 1848.

¹⁸ In 20 cases he observed three recurrences—one four weeks after the discharge of necrotic tissue, a second case six months after the first attack, the third case after three years. Babes and Zambitovici (Annal. de l'Institut. de Path. et de Bact. de Bucarest, 1895, v) refer to several cases.

Some writers advise applications of alcohol or hydrogen peroxide, or potassium chlorate, nitric acid, etc. Others advise cauterization of the ulcer with the actual cautery; still others practise excision of the diseased area. No matter what the treatment employed, only isolated cases have recovered. It is important to make frequent cultures from the necrotic areas, as diphtheria may closely simulate true noma.¹⁹ If there is any doubt as to the diagnosis, antitoxin should be given.

The bacteriology of noma rests on a definite basis since 1899, when Perthes²⁰ and Seiffert²¹ independently described a bacterium or group of bacteria in this disease. Although, up to the present time, Koch's laws have not been fulfilled²² the disease has not been experimentally reproduced and the bacteria have not been artificially cultivated—the constant presence of the bacteria in noma, and only in this disease, points very strongly to an etiological relationship. Perthes found that noma is due to a fungus-like growth belonging to the streptothrix group. At the border line between the gangrenous ulcer and normal tissue he found a thick branching network of fine fusiform threads—mycelium. From this mycelium single fine rods and spirilla extend into the normal tissue, surround the cells, and cause their death.²³ Krahn believes that the growth described by Perthes consists of two organisms—the spirillum sputigenum and spirochete dentium.²⁴ The majority of observers agree with Perthes and Seiffert. The same bacteriological picture was described in noma of other parts of the body by Matzenauer.²⁵ Perthes prepared his specimens for examination by treating the teased tissue or section from the edge of the ulcer—removed post

¹⁹ Hektoen, in the discussion on Bishop and Ryan's paper before the Chicago Pathological Society, pointed out the close clinical correspondence between their cases of noma and cases of gangrene of the skin in which the Klebs-Loeffler bacillus is found. And Loeffler, at a meeting of the Greifswald Medizinische Verein, in 1890, called attention to the similarity between pathological specimens from cases of noma, shown by Grawitz (Deut. med. Woch., 1890) and diphtheria in calves (Kälberdiphtherie) that he had observed.

²⁰ Arch. f. klin. Chir., 1899, lix.

²¹ Münch. med. Woch., 1901.

²² Hofman and Küster (Münch. med. Woch., 1901, 1907) found abscesses in animals after the bacteria were injected and found the same bacteria in the abscesses. Furthermore, they obtained (impure) anaerobic growths of the organism. Neither of these observations has been subsequently substantiated.

²³ Hanke (Jahrb. f. Kinderheilk., 1888, xxvii) and others have advanced evidence to show that the death of the cells is due to chemical influences.

²⁴ Miller (Microorganisms of the Human Mouth, 1890) has shown that these two organisms are normal inhabitants of the mouth, in small numbers. As all attempts at their cultivation have failed, he considers them parasites that cannot be separated from their hosts. In all forms of stomatitis, as well as in oral noma, these bacteria are present in enormous numbers in scrapings from the lesions. The fusiform "bacillus" of Vincent is also found on the surface of these ulcers. But it has not been demonstrated that any of these organisms are related to the streptothrix found in the tissues in noma, although some of the terminal filaments of the streptothrix resemble them closely (see Migula's (System der Bacterien, 1900) classification of these organisms).

²⁵ Archiv. f. Dermat. und Syph., 1902.

mortem—with dilute carbol-fuchsin for twenty-four hours and then briefly washing with alcohol.²⁶

The clinical and bacteriological pictures of the cases of noma in our epidemic correspond in good part with the description given above. However, some features of importance in our cases warrant a description of them in some detail; the detail of the spread of gangrene, the appearance of the streptothrix in individual cases,²⁷ etc., will be omitted. By "conservative" treatment we mean topical applications of peroxide of hydrogen, pure alcohol, and potassium chlorate; by "radical" treatment, thorough cauterization of the ulcer and of adjoining tissue with the actual cautery.

CASE I.—*Measles; ulcerative stomatitis; noma of the vulva; recovery.*

Jennie W., aged two years, was always delicate. Bilateral chronic otitis media. Measles March 9, 1909, complicated by a severe ulcerative stomatitis. The latter cleared up except for one ulcer. This necrotic area became gangrenous in its centre. A specimen removed did not show the streptothrix of noma. On March 17 a grayish membrane was observed covering the vulva and extending over the labia minora and across the perineum to the rectum. Cultures for diphtheria were negative; antitoxin had no effect. The membrane spread, the affected area became necrotic in forty-eight hours, and there was a profuse discharge of a gangrenous odor from the vagina and rectum. A specimen removed from the edge of the ulcer showed the streptothrix of noma. After two weeks, during which period the child was profoundly prostrated, the discharge diminished and the ulcer assumed a healthier appearance. Although there was a considerable loss of tissue, little deformity remained when healing was complete. Treatment was conservative. During convalescence the ulcer in the mouth slowly healed.

CASE II.—*Measles, ulcerative stomatitis; diphtheria of the vulva; oral noma; recovery.*

Marie F., aged two and a half years; was always well and strong. On March 10 measles developed, in the course of which ulcerative stomatitis appeared. March 16, a membrane was first noticed on the vulva similar to that in the first case. Cultures showed Klebs-Loeffler bacilli; the membrane disappeared after antitoxin injections. As the ragged sloughing ulcers about the teeth showed no signs of

²⁶ Weaver and Tunnick (Jour. Infect. Dis., 1907) demonstrated that this streptothrix is decolorized by Gram's method. They obtained the best staining reactions by dropping a 10 per cent. saturated solution of alcoholic gentian violet in 5 per cent. phenol on the section (that had been embedded in paraffin, treated with xylol, followed by absolute alcohol) for five minutes, clearing with aniline oil, washing with xylol, and mounting in balsam. A complete bibliography of noma is given by Weaver and Tunnick, *Journal of Infectious Diseases*, January, 1907.

²⁷ The streptothrix stained very well in our cases with the simple method of Perthes. I obtained the specimens by removing a small wedge of tissue from the edge of the ulcer, employing small straight scissors and forceps. A tonsillar "punch" may be employed to advantage.

healing, they were cauterized with the actual cautery on March 25. Following this all but one of the ulcers healed. The latter was situated near the right upper canine tooth; a section removed from it showed the streptothrix of noma. Treatment consisted of cauterization every second day. April 8, infiltration of the upper lip; ulcer much larger; superior maxilla exposed; overlying skin bluish. General condition good; slight fever and prostration. After fragments of the necrotic superior maxilla had separated, improvement began. The violaceous hue of the skin disappeared; the infiltration softened; and finally the slough separated from the ulcer. A specimen removed at this time showed numerous spindle-shaped rods extending into normal tissue, but no mycelium. The treatment was conservative from the time the gangrene began to spread.

CASE III.—*Measles; diphtheria; oral noma; recovery.*

Isidor L., aged two years, had been previously well and strong. Measles March 18, complicated by faucial diphtheria. The membrane disappeared a few days after antitoxin injections. About one week later an ulcer appeared about the upper incisors. Despite several cauterizations, it spread until a large piece of necrotic maxilla was exposed. Treatment by cauterization was then stopped. A specimen removed showed the typical streptothrix. The upper lip became exceedingly firm and infiltrated, but the skin remained unchanged. During a period of ten days this condition was stationary; the child was listless and apathetic, he had no fever, pulse was rapid. Then a large fragment of necrotic maxilla became detached and was removed. Thereafter the local and general condition improved. Treatment was conservative after the spread of the ulcer. Little deformity remained after healing was complete.

CASE IV.—*Measles; pneumonia; oral noma; death.*

Doris A., aged three years, was always pale and weakly. Enterocolitis in 1907, with recurrences from time to time. Measles March 8, complicated by a severe pneumonia. On March 17 an ulcer was seen on the mucous membrane of the right cheek. Cultures negative; antitoxin without effect; characteristic odor from the mouth. The cheek became indurated very rapidly, the overlying skin assumed the typical color, the ulcer spread to the vermilion border of the lip. The child died March 21, apparently overcome by toxemia. The treatment was conservative. A specimen was not removed.

CASE V.—*Measles; diphtheria; ulcerative stomatitis; oral noma; death.*

Harry S., always well and strong. Measles March 12; tonsillar diphtheria March 19. The latter yielded to antitoxin injections. A mild form of stomatitis was present. On March 23 a ragged ulcer appeared below the lower central teeth, where there had been no previous lesion. A section showed the streptothrix of noma. Thor-

ough cauterization was practised; the next day the adjoining maxilla was exposed and the submaxillary region was infiltrated. On March 25 an ulcer appeared about the teeth of the upper jaw exactly opposite the gangrenous lesion of the lower—apparently a contact infection. It spread rapidly, and the eyelids and lip became puffy; an offensive discharge issued from the nostrils. The upper lesion spread more rapidly than the lower. Temperature ranged from 100° to 104°; pulse very rapid and small. The gangrenous ulcers finally perforated the skin over the chin and over the upper lip; pus appeared in the diarrhoeal stool; the patient succumbed March 30.

CASE VI.—*Measles; pneumonia; ulcerative stomatitis; diphtheria; oral noma; death.*

Daniel B., aged three years; always ailing and on special diet for a year. Measles March 14; shortly after, a severe ulcerative stomatitis. Pneumonia with moderate prostration; convalescent by March 20. Faucial diphtheria on March 21, yielding to antitoxin injections. On March 23 an ulcer was first noted on the inner surface of the left cheek; at the same time a faintly gangrenous odor of the breath was observed. A section removed showed the lesion of noma. Although the ulcer was thoroughly cauterized, it spread and the overlying skin became necrotic; perforation occurred two days before death. The latter occurred on April 3 from a septic bronchopneumonia. This patient suffered considerable pain—an exceptional feature in our cases.

CASE VII.—*Measles; ulcerative stomatitis; oral noma; death.*

Eddie A., aged two and a half years; was always strong and well-nourished. Measles appeared March 6, complicated by ulcerative stomatitis of moderate severity. On March 18 an ulcer was first seen in the normal mucous membrane along the frenum linguae. With daily deep cauterization, this ulcer remained stationary, whereas the ulcers surrounding the teeth healed. A section taken from the sublingual lesion showed the streptothrix of noma; one removed from one of the other ulcers did not. On April 1 the ragged ulcer under the tongue began to spread on the surface and into the depths. It became gangrenous, spread over the whole floor of the mouth, and caused a marked induration in the submaxillary region. On April 4 an ulcer under the upper lip appeared, opposite the lower ulcer. It spread more rapidly than the original lesion. April 7, gangrene of the skin over both ulcers. Death on April 9.

CASE VIII.—*Measles; ulcerative stomatitis; oral noma; death.*

David R., aged two and a half years; always ailing and weakly. Had measles March 17, complicated by mild ulcerative stomatitis. March 22, apparently on the base of one of the ulcers about the lower central incisors there was a large deep ulcer. A specimen showed the streptothrix. The ulcer was frequently cauterized, and did not grow larger until April 4. It then began to spread, so that

by April 7 the chin was swollen and shiny. The next day a contact (?) lesion appeared on the upper gums and spread like the primary ulceration. A specimen removed showed the same pathological picture as that from the lower lesion. The skin of the chin became gangrenous, and soon after, gangrene of the upper lip developed. The patient died April 11; he was not prostrated until twenty-four hours before death.

In the last three cases frequent cauterization was employed after the ulcers had begun to spread, in order to determine its value in this stage of the disease. This radical treatment had no salutary effect on the lesion; if anything, it appeared to hasten the spread of the gangrene.

To these undoubted cases of noma I would add the three cases to which reference has already been made. All three patients had measles, and in two of them ulcerative stomatitis developed. In both the stomatitis cleared up with the exception of one ulcer. In the third case there was a single ulcer from the outset. The ulcer, in each case, was deep, ragged, and necrotic, identical with the ulcer observed in the pre-gangrenous stage of noma. Specimens taken from the edge of the ulcer showed in each case the streptothrix of Perthes. The ulcers were submitted to frequent and thorough cauterizations, and after a period of two to four weeks they healed without any spread of necrosis and without the development of serious constitutional symptoms.

Among the patients with stomatitis there were several who had very suspicious ulcers. Specimens removed did not show the streptothrix, and none of these patients developed noma.

It will have been noted that for the cauterizations and for the removal of specimens no anesthesia was employed. This was done for the following reasons: In the first place the manipulations may be carried out quite painlessly. In the second place, these children are already much weakened by their disease, and the function of their lungs is impaired by the associated pulmonary affection; in them a general anesthesia must certainly be very dangerous. In not a few of the patients who were operated upon under general anesthesia septic pneumonia followed.

In Cases II, VII, and VIII, the spread of gangrene was delayed about two weeks, in each case, by repeated cauterizations, and I believe that if cauterization had been begun earlier, the spread of noma might have been much longer delayed. It cannot, of course, be proved that the three cases of ulcer identical clinically and histologically with the pre-gangrenous ulcer of noma were really cases of noma aborted by radical treatment; the findings, however, all point in that direction. It appears to me, from our experience, that the radical treatment is of value only in the pre-gangrenous stage of noma. We have found the streptothrix in this stage, and hence have concluded that it is unnecessary to wait for the appearance of gan-

grene in order to institute radical treatment. As before stated, actual cauterization is as effectual as excision and is less mutilating.

The close association of noma with ulcerative stomatitis was seen in this epidemic. Ulcerative stomatitis of varying severity was present in 8 of the 11 patients; in some of the cases the ulcers were necrotic, almost gangrenous. Yet in only one (Case VIII) did it seem probable that noma had developed on one of the lesions of ulcerative stomatitis. From the observation of all the cases in this epidemic, and from the microscopic studies, we must conclude that disease of the mouth prepared a favorable soil for the development of noma, but that there was no evidence of a direct etiological connection between stomatitis and noma.

What significance should be attached, in Cases V, VII, and VIII, to the development of gangrenous ulcers—apparently by contact—cannot be determined. Such a path of transmission of the disease would seem probable; it occurred in three of our five fatal cases. In one of these patients the microscopic examination revealed the streptothrix in sections from the second ulcer. I have been unable to find any mention in the literature of second ulcers in noma.²⁸

CONCLUSIONS. Noma usually appears in epidemic form; its contagiousness has not been proved. The disease is an entity, and not a later stage of ulcerative stomatitis; the latter offers a good soil for the development of noma. There is regularly present in noma a streptothrix characterized by a thick meshwork of mycelium at the border line between normal and necrotic tissue; fine rods and spirilla extend from mycelium into the adjacent tissues. The constant presence of this streptothrix, to the exclusion of other organisms, indicates that, in all probability, it stands in direct etiological relationship to noma. The streptothrix is present in noma before the disease is fully manifest—in the pregangrenous stage. It is in this stage of the disease that radical treatment is to be practised; after the ulcer spreads, the best results are obtained by conservative measures. General anesthesia should not be employed in any form of treatment because of the pronounced tendency to the development of septic pulmonary disease.

²⁸ Blood examinations were made in four cases. There was a marked anemia (2,000,000 red cells), with decided poikilocytosis and anisocytosis; no leukocytosis. The blood drop was very watery and was expressed with difficulty. Cells resembling myelocytes were present in the spreads. In three patients Wassermann tests were kindly made by Dr. Kaplan, bacteriologist to the Montefiore Home, with negative results. They were done because it has been suggested that the organism of noma is in the same class as *Treponema pallidum*.